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10/751,072	01/02/2004	Sven Eyckerman	2676-6264US	2266

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EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/751,072	EYCKERMAN ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-22* is/are pending in the application.

4a) Of the above claim(s) *9,10,12,14 and 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,11,13,15,16 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1 and 3-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 11/2/05 has been entered in full. Claims 1, 16 and 22 are amended. Claims 2 and 23 are canceled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains claims 9, 10, 12, 14, 17-21 drawn to an invention nonelected without traverse in Applicant's response filed 5/6/05. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1, 3-8, 11, 13, 15, 16, 22 are under consideration in the instant application.

Priority

Acknowledgement is made of the certified copy of the priority document EPO 01202569.8 filed 11/25/05 by Applicants.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (7/29/05).

The objection to claim 2 is *withdrawn* in view of the cancellation of the claim.

All rejections of claims 2 and 23 are *withdrawn* in view of the cancellation of the claims.

The rejection of claim 16 under 35 U.S.C. 112, first paragraph at pg 6-7, as failing to comply with the written description requirement (new matter) is *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 1, 3-8, 11, 13, 15 and 16 under 35 U.S.C 112, 2nd paragraph at pg 7-8 as being indefinite for failing to particularly point out and distinctly

claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to claims 1 and 16.

Please see new claim objections and rejections, below.

Double Patenting

Claims 1, 3-8, 11, 13, 15, and 22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7, 12, 14 and 16 of copending Application No. 10/303157 in view of U.S. Patent No. 5,885,779 and in further view of Nicholson et al, published June 6, 2000 (PNAS 97(12): 6493-6498). This provisional rejection was set forth previously at pg 3-6 of the 7/29/05 Office Action.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Applicants' arguments (11/2/05; pg 6-9) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 11/2/05, Applicants submit that the instant claims are not obvious over the claims of the '157 application in view of the '779 patent and in further view of Nicholson et al. Applicants submit the '157 application teaches an inactivated recombinant receptor that can only be activated by combination of 1) ligand binding to extracellular binding domain and 2) prey binding to cytoplasmic bait domain. Applicants submit that because this receptor is in default inactivated condition, the substitution of an inhibitor for the activator would not work in the claimed invention.

Applicants' arguments have been fully considered but are not found persuasive. It is true that the '157 application teaches a chimeric receptor wherein the receptor is inactive unless bound by ligand and prey polypeptide. However, one of skill in the art

would have been motivated to substitute a receptor with an activation site for the following reasons.

Nicholson teaches a chimeric receptor (EPOR-gp130) comprising a gp130 cytoplasmic domain in which tyrosine-757 has been mutated to phenylalanine (Y757F; pg 6496). The receptor taught by Nicholson still contains an "activation site" because it is activated by ligand to 4-fold higher levels than the chimeric receptor without the Y757F mutation. Higher expressed levels of SOCS3 are required to inhibit STAT3 activation by the mutant receptor.

As set forth previously, the '779 patent teaches (column 3, starting at line 60) advantages of using a system that relies on activation of a reporter to indicate disruption of bait-prey interaction, including avoiding relying on loss of a signal to indicate bait-prey disruption.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the gp130 (Y757F) cytoplasmic domain taught by Nicholson for the cytoplasmic domain of the receptor taught by the '157 application. The recombinant receptor thus produced would have the characteristic of being inhibited by a prey fusion protein comprising a SOCS3 protein. The person of ordinary skill in the art would be motivated to use the gp130 (Y757F) cytoplasmic domain in the recombinant receptor because the '779 patent teaches that systems that screen for compounds that disrupt protein-protein interactions reduce false positives. Using a receptor comprising a gp130 domain taught by Nicholson with a prey-SOCS3 fusion would produce a receptor-based system where disruption of the protein-protein (bait-prey) interaction leads to activation. One would have expected success because tethering SOCS3 to the mutant gp130 receptor by means of the bait-prey interaction would restore SOCS3 to its correct cellular milieu, causing inhibition of JAK signaling.

It would further have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the recombinant receptor as taught in claims 2-5 and 7 of 10/303157, to produce a receptor as taught by these claims but wherein the receptor is inhibited by binding of a prey molecule. The person of ordinary skill in the art would be motivated to include an inhibitor for the same reasons as discussed above

and because the further teachings of claims 2-5 and 7 are modifications of the receptor that allow for versatility in the type of receptors or bait used, and one would have expected success because, in the absence of other evidence, a receptor that is inhibited by prey binding would work just as well with these modifications as a receptor that is activated by prey binding.

It would further have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the vectors or eukaryotic host cell as taught in claims 12, 14 and 16 of 10/303157, to produce a vector that encodes a receptor that is inhibited by prey binding, or a host cell comprising said vector. One would have been motivated to do so because of the motivation to produce a receptor that is inhibited by prey binding as described above, and because a vector and host cell is necessary to produce such a receptor, and one would have expected success because, in the absence of other evidence, such a vector or host cell would be expected to work just as well to produce a receptor inhibited by prey binding as a vector or host cell that produces a receptor that is activated by prey binding.

This is a provisional obviousness-type double patenting rejection. It is noted that the issue will become moot for the first of the two cases to be found allowable, see MPEP 804. However, Applicants are cautioned that any argument of the above rejections should not be delayed; argument of the double patenting rejection after prosecution has otherwise concluded will not be considered as being timely. The only actions that will be deemed appropriate at such time as claims are found otherwise allowable will be cancellation of claims or filing of a terminal disclaimer.

Claim Rejections - 35 USC § 102

Claims 1, 3-5, 11, 13, 15, 16 and 22 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Medici et al, 1997 (The EMBO Journal. 16(24): 7241-7249).

Applicants' arguments (11/2/05; pg 10-11) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 11/2/05, Applicants submit that the claims as amended include the limitation that the cytoplasmic domain of the receptor must comprise "at least one activation site". Applicants argue that Medici does not teach a receptor with cytoplasmic domain comprising an activation site. Applicants argue that the activation site of the GPCRs taught by Medici is on the G-protein. Applicants argue that it is not inherent that a prey polypeptide comprising an inhibitor would inhibit activation of the receptor taught by Medici. Applicants argue, "Medici fails to disclose any bait proteins on the cytoplasmic domain" of the GPCRs, and the "effect of a prey polypeptide comprising an inhibitor bound to the receptor of Medici would not be inherent – it would likely have no effect."

Applicants' arguments have been fully considered but are not found persuasive. The specification defines "activation site" on pg 14, paragraph 59 as "the site that, in the wild type receptor, is modified after binding of a ligand to the ligand binding domain, thus leading to a reorganization of the receptor and subsequent activation of the modifying enzyme activity and to which a compound of the signaling pathway can bind after modification, or any site that can fulfill a similar function." This definition does not limit the form of modification of the "activation site", and therefore modification encompasses a broad range of modifications, e.g. phosphorylation or a conformation change. Finally, it is noted that "modifying enzyme activity" is defined as "the enzymatic activity associated to or incorporated in the cytoplasmic domain of the receptor that is normally induced upon binding of the ligand to the ligand binding domain and subsequent reorganization of the receptor and may modify the activation site" (pg 14, paragraph 60).

The Ste2 receptor taught by Medici has a site in the cytoplasmic domain that is encompassed by the above definition of "activation site". Specifically, the Ste2 receptor has a cytoplasmic recognition site for the G-protein Gpa1 (see Figure 6, pg 7246 and the Discussion section from page 7246-7247). Ligand binding induces a conformation change that allows this recognition site to interact with the C-terminus of the G protein, and subsequent GDP/GTP exchange (which meets the definition of "modifying enzyme activity"). It is maintained that the limitation of "wherein the activation of said

recombinant receptor is inhibited by binding of a fusion protein to said heterologous bait polypeptide" is an inherent characteristic of the receptor described by Medici. For example, any other fusion protein comprising Protein Y would inhibit (i.e., disrupt or reduce) the interaction between the GPCR-bait (Protein X) fusion protein and the G-protein-prey (Protein Y) fusion protein, resulting in inhibition of activation of the receptor (see Figure 6).

Because claim 1 as amended still encompasses the chimeric receptor taught by Medici, dependent claims 3-5, 11, 13, 15, 16 and 22 remain anticipated by Medici for the reasons set forth previously at pg 9 of the Office Action of 7/29/05.

Claim Rejections - 35 USC § 103

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Medici et al, 1997 in view of Osborne et al, 1995 (cited by the Applicant in the IDS submitted 6/24/04).

Applicants' arguments (11/2/05; pg 11-12) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 11/2/05, Applicants submit that Medici in view of Osborne does not teach a receptor with "at least one activation site". Applicants further argue that a person of skill in the art would have no motivation to combine the references or any expectation of success from combining the references, because 1) Medici is investigating membrane bound receptors in yeast, while Osborne is using normal nuclear based yeast two-hybrid and studying protein expression at the cytoplasmic level; 2) Osborne's protein expression requires overexpression of kinase in yeast which would prove toxic in mammalian cells as used in the instant invention; and 3) there are no cytokine or tyrosine kinase type receptors in yeast.

Applicants' arguments have been fully considered but are not found persuasive. As described above in the section entitled "Claim Rejections – 35 USC § 102", the receptor taught by Medici contains a site meeting the definition of an activation site; therefore, claims 6-8 remain unpatentable over Medici in view of Osborne as set forth at pg 10-11 in the 7/29/05 Office Action. In response to applicant's argument that there is

no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it is noted that the systems of Medici and Osborne both use yeast cells. Applicants' claims are not restricted to mammalian receptors or cells; therefore the instant claims encompass yeast receptors and cells. It is not relevant whether or not Osborne's protein expression would prove toxic in mammalian cells, because one skilled in the art would combine Medici and Osborne for use in yeast cells. The person of ordinary skill in the art would have been motivated to make that modification because Medici teaches (pg 7247) the advantage their recombinant receptor can be used as a two-hybrid system to investigate protein-protein interaction on the cytoplasmic side of the cell membrane. The Examiner is unclear how Applicants' statement "there are no cytokine or tyrosine kinase type receptors in yeast" impacts the motivation to combine the methods of Medici and Osborne, both of which use yeast proteins and yeast cells, with no requirement for cytokine or tyrosine kinase type receptors.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JANET L. ANDRES
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